Estrogen Status Alters Tissue Distribution of Oral Dose of ^{75}Se-Selenite and Enhances Hepatic Levels of SelP mRNA, GPx mRNA, GPx activity and Se

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ABSTRACT

An association between male and female sex hormones and selenium (Se) status has been reported in animals and humans. These relationships may be important relative to the use of selenium in hormone related diseases such as breast cancer. The purpose of this study was to examine the effect of estrogen status on the tissue distribution of Se and mRNA levels of selenoprotein P (SelP) and glutathione peroxidase (GPx) in liver. 60 μCi of ^{75}Se as selenite was orally administered to each bilaterally ovariectomized rat 5 weeks after implantation with either placebo pellet (OVX) or pellet with estradiol (OVX+E2). Blood and tissues were collected 1, 3, 6, and 24 h after dosing. Differences ($P<0.05$) in ^{75}Se in blood, liver, heart, kidney, spleen, brain, and thymus were noted at certain times. Plasma SelP in OVX+E2 group contained a greater percentage of ^{75}Se at 3, 6 and 24 h compared to OVX group ($P<0.05$); ^{75}Se in plasma GPx also was greater in OVX+E2 compared to OVX group at 24 h ($P<0.05$). Real-time RT-PCR analysis showed that both hepatic SelP mRNA (0.93 vs. 0.50) and GPx mRNA (2.81 vs. 2.24) were significantly greater in OVX+E2 group than in OVX group. These results suggest that estrogen status affects distribution of ingested Se in tissue- and time-dependent manners, as well as the expression of hepatic SelP and GPx at both protein and mRNA level.

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INTRODUCTION

- Relationships between gender/sex hormones and Se status have been observed in animals and humans.
- Preliminary findings from our laboratory strongly support the relationship between estrogen and tissue Se status.
- Insights about impact of estrogen on distribution and metabolism of Se in multiple tissues are limited.
- We **hypothesize** that estrogen status will affect metabolism of ingested ^{75}Se-selenite as well as the hepatic levels of SelP and GPx mRNA.
- The **objective** of this study was to examine the effect of estrogen status on tissue distribution and metabolism of Se at both mRNA and protein levels in a rat model.
- The results of this study are important when considering the use of Se in the prevention or treatment of hormone-related diseases such as breast cancer.

ACKNOWLEDGEMENTS

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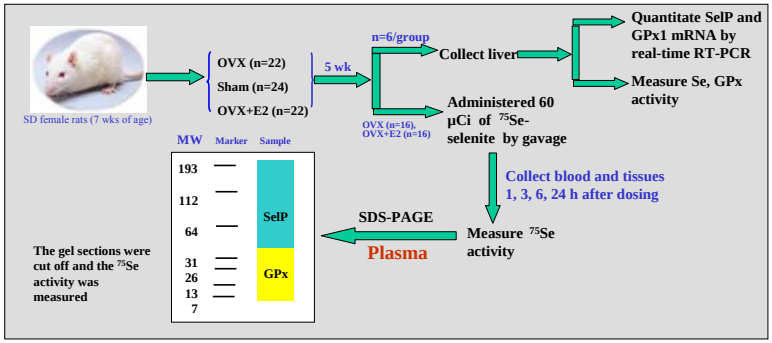
METHODS



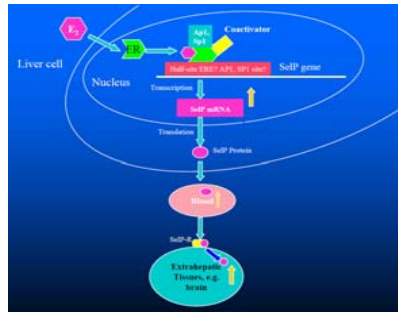


Figure 5 A hypothetical model of estrogen regulation whole-body Se metabolism

RESULTS

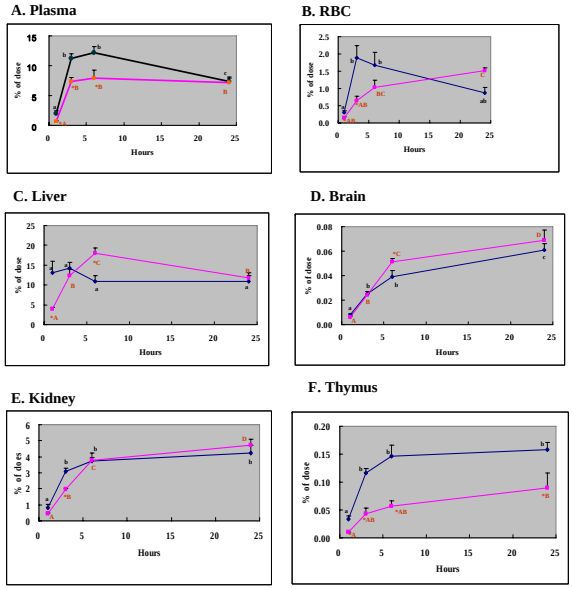


Figure 1 ^{75}Se activity in tissues at 1, 3, 6, and 24 h after administration 60 μCi ^{75}Se-selenite by gavage. Ovariectomized rats were implanted with either placebo (OVX) or estradiol (OVX+E2). Data are Means ± SEM (n=4 per time in each group). Statistically significant differences ($P<0.05$) between OVX group and OVX+E2 group are denoted by presence of an asterisk (*). Within the same treatment (OVX/OVX+E2), means that do not share the same letter are significantly different at $P<0.05$. Panel A, plasma; Panel B, RBC; Panel C, liver; Panel D, brain; Panel E, kidney; Panel F, thymus. Red line: OVX+E2, Black line: OVX

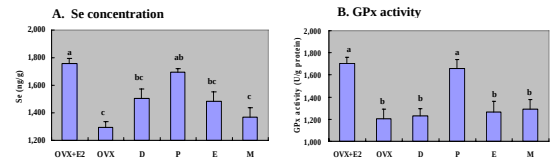


Figure 2 Effect of estrogen status on hepatic Se concentration (**Panel A**) and glutathione peroxidase (GPx) activity (**Panel B**) in female SD rats. Test groups include OVX with estrogen replacement (OVX+E2), OVX with placebo replacement (OVX), sham-operated with placebo replacement in diestrus (D), proestrus (P), estrus (E), and metestrus (M) stages. Data are Means ± SEM (n=6). Presence with different letters above each bar indicate significant differ ($P<0.05$).

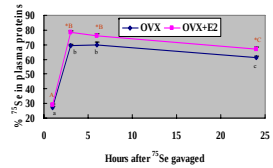


Figure 3 ^{75}Se activity in plasma SelP 1, 3, 6, and 24 h after administration 60 μCi ^{75}Se-selenite by gavage. Animals are ovariectomized rats receiving either placebo pellet (OVX) or pellet with estradiol (OVX+E2). Data are Mean ± SEM (n=4). Statistically significant difference ($P<0.05$) between OVX group and OVX+E2 group are denoted by presence of an asterisk (*). Within the same treatment (OVX/OVX+E2), means do not share the same letter differ significantly ($P<0.05$).

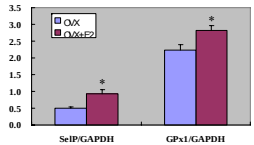


Figure 4 Estrogen replacement in OVX rats increases hepatic levels of SelP and GPx1 mRNA. RT reaction was carried out with extracted RNA isolated from liver of OVX rats receiving estrogen replacement (OVX+E2) and OVX rats with placebo pellet (OVX). Real-time qPCR was performed using an Mx3000P QPCR® system. mRNA levels were normalized by GAPDH. Data are Means ± SEM for 6 animals in each group. * $P<0.05$ between OVX and OVX+E2 by Student's t test

SUMMARY AND CONCLUSIONS

- **Estrogen enhances ^{75}Se transport into liver from 1 to 6 hour, and facilitates ^{75}Se to extra-hepatic deposition after 6 hour.**
- **The decrease in plasma 75Se-SelP from 6 to 24 h suggests that SelP was delivering ^{75}Se to other tissues.**
- **Estrogen increased Se content and GPx activity in liver.**
- **Estrogen up-regulated SelP and GPx mRNA expression in liver.**
- **Conclusions: Up-regulation of SelP expression in liver has special significance of whole-body Se metabolism due to the transport function of SelP. Estrogen appears to enhance transport of hepatic Se to selected tissues via increased expression of SelP mRNA and subsequent synthesis and excretion of SelP.**

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